EXHIBIT 20

EXPERT REPORT

Child: A.S.

Dr. Nathaniel Halpern Robin

September 28, 2017

1. **Credentials**

1.1 My name is Dr. Nathaniel Halpern Robin. I am a tenured Professor in the Department of Genetics at the University of Alabama At Birmingham. I am currently licensed to practice medicine in the state of Alabama and am a Diplomat, American Academy of Pediatrics and a Diplomat, American Board of Medical Genetics, Clinical Genetics. A copy of my CV is attached as appendix A. to this report.

1.2 Clinical Genetics is the medical specialty which provides diagnostic services and "genetic counseling" for individuals or families with, or at risk of, conditions which may have a genetic basis. These include

- Chromosomal abnormalities, which cause birth defects, mental retardation and/or reproductive problems.
- Single gene disorders such as cystic fibrosis, muscular dystrophy, Huntington's disease and sickle cell disease.
- Familial cancer and cancer-prone syndromes such as inherited breast or colorectal cancer and neurofibromatosis.
- Birth defects which may possibly be related to a genetic component such as neural tube defects, cleft lip and palate, cognitive impairment, developmental delay, facial dysmorphism, hearing disorders and others.
- The elimination of genetic factors as a cause of certain birth defects through diagnostic testing, family history and environmental factors.

1.3 Individuals who are seen at the genetic clinic include parents with children with birth defects and/or learning disabilities who have been referred and investigated for genetic

factors. Individuals identified through childhood or pregnancy screening programs also require genetic services. Testing for genetic factors that affect drug prescribing is also part of our program.

1.4 Physicians and counselors are a vital part of the healthcare team that work closely with patients to provide a complete understanding of specific genetic concerns. The clinical genetics health care team provides information and support for individuals indicated for prenatal diagnosis, with an elevated risk for disease or birth defects, or with an undiagnosed genetic condition. The Genetics and Dysmorphology Clinic offers a means for diagnosis of birth defects and genetic disorders. Children and adults, with indications such those enumerated above are seen in a compassionate and caring environment in which the primary concern is that the needs of the family are met.

2. Materials reviewed and relied upon in preparation for this report:

My review includes the following:

- The medical of records of Martha Sansone, including but not limited to the records of Dr. Patti Nemeth of the Brain and Spine Center in Chesterfield, Missouri.
- The medical records of A.S. including but not limited to the medical records of Dr. James Gerst; Dr. J. Marsh, Dr. John Mantovani, Dr. Tyler Reimschisel.
- The depositions of Dr. Reimschisel and Dr. Marsh.
- The school records of A.S.
- The deposition of Mrs. Sansone, the biological mother of A.S.

- The relevant peer reviewed literature and studies regarding the medications prescribed to and taken by Ms. Sansone at the time she became pregnant with A.S.
- The reports of Dr. David A. Kessler, dated January 27, 2016, Dr. Michael Privitera of January 30, 2017, and Dr. Linda Motyka dated September 26, 2017.

I reviewed these reports as a source for information regarding additional peer reviewed articles to consult. I do not rely upon the opinions set forth in these reports as a basis for my opinion as the cause of the Major Congenital Malformations suffered by A. S.

In addition to the above, I rely on my education, training and experience in arriving at the opinions set forth below.

3. **Relevant Medical History of Marthee Sansone**

3.1 According to the records of Dr. Nemeth, Ms. Sansone, suffered from Complex partial seizures. While pregnant with her first child Ms. Sansone was on 250 BID of Depakote. This dosage remained for the first 7 months of her pregnancy. Her dosage was increased to 500 mg BID in the last two months of her pregnancy. Ms. Sansone delivered a healthy baby boy. This child has no malformations or learning disabilities.

3.2 Subsequent to this pregnancy Ms. Sansone's Depakote levels were increased to 750 mg BID. Since Ms. Sansone had expressed a desire to again become pregnant, 25 mg QOD of Lamictal was also prescribed with the intention of transitioning her from Depakote to Lamictal. On 2/10/24, after seizure episodes, the Depakote dosage was increased to 1000 mg BID. On 3/08/04 Ms. Sansone complained of nausea and dizziness. She was taken off the Lamictal. It was noted that because she could not tolerate the Lamictal she would remain on

Depakote and the Lamictal would be discontinued. According to the records, at that time her Depakote dose was increased to 1500 BID

3.3 On 8/04/04 Ms. Sansone reported to her neurologist that she was pregnant. At that time, her Depakote dose was noted to be 1000 mg BID. On 9.02/04 an additional 500 mg of Depakote was added to her dosage. On 9/22/04 it is noted in her neurology records that she is three months pregnant and her she is taking 1500 mg of Depakote. She remained on this dosage until A.S. Was born on [redacted]. It is also noted elseward in the records that Ms. Sansone smoked one pack of cigarettes a day during her pregnancy. And that she carried A.S. low in the pelvis.

4. Medical History of A.S

4.1 A.S. was born with congenital metopic craniosynostosis. His birth weight was pounds 14 ounces. Birth length was 18 inches. At four months of age A.S. underwent a release of the metopic craniosynostosis with bilateral frontotemporal and superior orbital reconstruction.

4.2 On July 26, 2005 A.S. was referred by Dr. Marsh to St Louis Child Neurology Services, for neurological consultation. Dr. John Mantovani noted, among other things, that as part of the comprehensive evaluation, A.S. had a CT scan including three-dimensional surface rendered reconstruction showing unremarkable brain structure and metopic synostosis.

4.3 It was noted that at four months of age he was not yet rolling over and he did not smile. It was also noted that the family history was negative for neurological or developmental disorders with the exception of maternal epilepsy. The diagnosis on that exam lists metopic synostosis with borderline microcephaly, mild-moderate developmental delay in terms of social responsivity, muscle tone and head control and in-utero exposure to maternal valproic acid.

4.4 On January 4, 2006 A.S. was again evaluated by St Louis Child Neurology Services. It was noted by Dr. Montavani at that visit the medical history of A.S. was complicated by maternal treatment with Depakote during pregnancy. Dr. Montavani provided a diagnosis of developmental encephalopathy with mild microcephaly and global developmental delay.

4.5 On September 26, 2006, A.S. was again seen by Dr. Mantovani and at that time it was noted that A.S has small dysmorphic features and OFC of 43 cm which was markedly microcephalic. He had atypical facial features with trigonencephaly, prominent epicanthal folds, thin extended eyebrows, depressed nasal bridge, anteverted nostrils, very long philtrum and a thin vermillion and thin, rather tapered fingers. Dr. Montavani diagnosed A.S. as having developmental encephalopathy with microcephaly and developmental delay and physical features suggesting fetal valproic acid syndrome. It was suggested to the mother by Dr. Mantovani that she consider a genetics consultation for an opinion regarding fetal valproic acid syndrome. It was also noted in the neurodevelopmental prognosis of A. S. - current microcephaly that the mother's head circumference is just above the 2nd percentile for an adult woman.

4.6 On November 7, 2007, Dr. Mantovani again re-evaluated A.S. and at that time recorded his diagnosis as Fetal Valproic Acid Syndrome and Global Developmental Delay – mild to moderate.

4.7 As per the recommendation of Dr. Mantovani, Mrs. Sansone sought a neurogenetics consult. On March 8, 2007 A.S. was seen and evaluated by Dr. Tyler Reimschisel, a neurogeneticist practicing at the St Louis Neurogenetics Clinic. Dr. Reimschisel took a complete family medical history, and a medical history of A. S. He conducted a physical exam as well. Dr. Reimschisel noted that A.S. was not exposed to alcohol or other drugs during the pregnancy; that he has a brother who is heathy; that, there is no other significant family history

of birth defects craniosynostosis, learning disabilities, developmental problems, infertility or other childhood disabilities. The assessment of Dr. Reimschisel was that he agreed with the opinion of Dr. Mantovani that A.S.'s presentation was consistent with valproic acid exposure in utero. While he noted in his letter to Dr. Mantovani that valproic acid exposure does not increase the rate of craniosynostosis, when he gave sworn testimony Dr. Reimschisel stated that this statement was in error and that upon further investigation he discovered that the literature does state that there is an association with valproic acid exposure in utero and the malformation of craniosynostosis as the literature provided in the report substantiates that statement. *Etiopathogenesis of craniosynostosis. Neurosurgery clinics of North America*, 01 Jul 1991 2(3); 507-513. Cohen MM Jr. Jentink et al (2010) Valproic Acid Monotherapy in Pregnancy and Major Congenital Malformations N Eng J Med 362:2185-93.

4.8 On November 9, 2012, A.S. was seen by Dr. Jeffrey L. Marsh, the plastic surgeon who performed his initial surgery. It was noted that A.S. wears glasses, he looks moderately dysmorphic, head circumference = 47.5 cm (3%), medial canthal distance – 28 mm (35%), interpupillary distance e 47 mm (25%0. The maxillary mandibular teeth are splayed. There was mild ankyglossia. A. S. weight was 56 lbs. (50%) Height 49 in (50%). He had a pediatric audiology exam on this date as well. This revealed mild hearing loss for the right ear 500-4000 HZ for the right ear and mild hearing loss 500-1000 Hz for the left ear.

4.9 It was noted in the records of November 9, 2012 that A.S. received special education resources, speech therapy and occupational therapy. Concerns were noted regarding his eating and drinking. It was noted that he uses fingers to move food around in his mouth with some limited movement of the tongue. It is also noted that A. S. will require orthodontics and

that he demonstrates open mouth posture at times and some drooling. It was noted that A.S. has phonemic repertoire below age expectancies.

5. Depakote (also referenced as Valproic Acid; Valproate; VPA) causes Fetal Valproate Syndrome, major malformations, myotopic craniosynostosis, dysmorphic features, developmental delay and learning disabilities and other birth defects.

5.1 Maternal use of Depakote during the first trimester of pregnancy is established as a cause of fetal valproate syndrome, major malformations including craniosynostosis, dysmorphic features, developmental delay, learning disabilities and other birth injuries associated with these conditions. "In children born with fetal valproate syndrome, it is important to be aware of the possibility of metopic suture synostosis, which we believe should be considered part of the syndrome, because early surgical intervention may improve cognitive outcome." *Craniosynostosis and fetal exposure to sodium valproate*; *J. Neurosurg* 2001 Nov. 1995 (5) 778:82 Lajeunic E, Barcik U, Thorne JA. Depakote is a human teratogen at recommended doses. Reports of the risk of fetal exposure to valproic acid.

5.2 Maternal use of Depakote presents a very high risk of overall birth defects. To quote the recent Valproate Patient Guide of January 2016 – published by the pharmaceutical company distributing Depakote:

> "If you take valproate when you are pregnant it can harm your unborn child. The risks are higher with valproate than with other medicines used to treat epilepsy. The risks are there whatever dose of valproate you take and the higher the dose the higher the risk The risks are then when valproate is taken alone and when it is taken with other epilepsy medicines. Taking valproate whilst pregnant can harm your child in two ways – it can cause birth defects and problems with development and learning."

6. Depakote causes Fetal Valproate Syndrome

Fetal valproate syndrome (FVS), is an anticonvulsant drug-related embryofetopathy that can occur when a fetus is exposed to valproic acid (VPA), characterized by distinct facial dysmorphism, congenital anomalies, including metopic Craniosynostosis and developmental delay (especially in language and communication.

6.1 Dysmorphic features

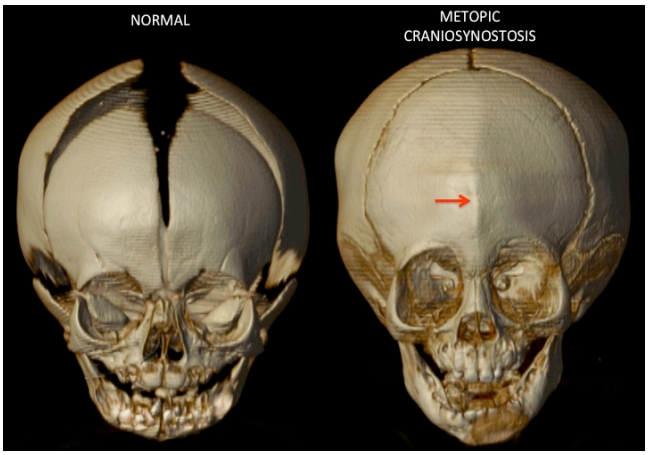
6.1.1 Dysmorphic features occur when a bodily structure of the fetus is not formed correctly. Children born to women who ingested Depakote (VPA) while pregnant may be born with dysmorphic features as part of the Fetal Valproate Syndrome. Features consistent with dysmorphism due to fetal valproate syndrome may include: eyes spaced too wide or too narrow, prominent epicanthal folds, thin extended eyebrows, depressed nasal bridge, anteverted nostrils, very long philtrum and a thin vermillion and other misaligned or structural anomalies.

6.1.2 Depakote is known to cause dysmorphic features in children born to women who took valproate acid while pregnant.

6.2 Metopic Craniosynostosis

6.2.1 The metopic suture separates the two frontal bones at birth and is the first skull suture to close physiologically, starting as early as at 3 months and generally being completely fused at the age of 8 months A premature fusion however, results not only in an obvious ridge over the midline of the forehead due to ossification of the suture, but also in a lateral growth restriction of the frontal bones. The end product is a skull with a triangular forehead, a bony midline ridge and a shortening of the anterior cranial fossa. Often there is some degree of soft tissue excess along the same line. The orbits are teardrop shaped and angulated towards the midline of the forehead Vertical growth restriction as expressed in reduced auricular head height

is one of the most significant components of the midline growth anomalies. Since the growth restriction results in a reduced intracranial volume, surgery is indicated to restore the scull volume as well as its appearance.



6.2.2 Depakote is known to cause metopic craniosynostosis in children born to women who took valproate while pregnant.

6.3 Cognitive impairment and developmental delay

6.3.1 Multiple studies indicate the causative relationship between the ingestion of Valproate Acid by women while pregnant and cognitive impairment and developmental delay in their exposed children. Wyszynske, MD, PhD; M. Nambisan, et al. *Increased rate of major malformations in offspring exposed to valproate during pregnancy*. Neurology 2005; 64:961-965. Vol. 31, No. 42; Centers for Disease Control, Morbidity and Mortality Weekly Report, August 26, 1983, 32(33); 438-9).

6.3.2 Abbott Pharmaceuticals, the major manufacturer and distributor of Valproate Acid (Depakote) in its updated 2016 patient guide also acknowledges that maternal use of valproate significantly increases the risk, not only of major congenital malformations, but also impaired cognitive development." Studies also indicate that offspring of mothers treated with

greater than 1000mg/day of VPA are at an increased risk, in particular of neural tube defects but also of other MCM's.

6.3.3 In utero exposure to antiepileptic drugs (AEDs) also is known to pose an increased risk of poorer cognitive abilities and developmental delay and this is especially associated with the use of valproate over other AED's. Bromley, Rebecca L. "*Early Cognitive development in children born to women with epilepsy: a prospective report* "Elpilepsia: Jones et al., 1989; Adab et al. 2004; "Consistent with findings regarding malformation incidence, the largest risk appears to be associated with exposure to sodium valproate." Adab et al., 2004; Bromley ET. al. 2009; Meador et al., 2009.

6.3.4 The specific risks of these MCM's and their association with VPA are further summarized by Abbott Pharmaceuticals in its handbook for physicians of January 2016:

> This booklet provides up-to-date information about the risk of neurodevelopmental disorders in children of women who have taken valproate during pregnancy in addition to the known risk of congenital malformations in exposed babies. Id. at pg. 3
> **1. Congenital malformations -** Data derived from a meta-analysis (including registries and cohort studies) has shown that 10.73% of children of women with epilepsy exposed to valproate monotherapy during pregnancy suffer from congenital malformations (95% CI: 8.16 -13.29), which represents a greater risk of major malformations than for the general population, for whom the risk is equal to about 2-3% Available data show the risk is dose dependent. The risk is greatest at higher doses (above 1g daily). A threshold dose below which no risk exists cannot be established based on available data. The most common types of malformations include neural tube defects, facial dysmorphism, cleft lip and palate, craniostenosis, cardiac, renal and urogenital defects, limb defects (including bilateral aplasia of the radius), and multiple various body systems *119036 Valproate HCP Booklet_Final_V2.indd 4 22/ January 2016.*
> **2. Developmental disorders -** Exposure to valproate in utero can have adverse effects on mental and physical development of the exposed children. The risk seems to be dose-dependent but a threshold dose below which no risk exists, cannot be established based on available data. The exact gestational period of risk for these effects is uncertain and the possibility of a risk throughout the entire pregnancy cannot be excluded. Studies2–5 in preschool children exposed in utero to valproate show that up to 30-40% experience delays in their early development such as talking and walking later, lower intellectual abilities, poor language skills (speaking and understanding) and memory problems. 119036 Valproate HCP Booklet_Final_V2.indd 4 22/01/2016 1

7. Dose Response

Mrs. Sansone was on doses of valproate at or exceeding of 1500 mg per day. Doses in this range are associated with an increased likelihood of MCM including craniostenosis as well as other birth defects. The Meador study demonstrated a dose-dependent effect for VPA on total serious adverse outcomes. The rate of serious adverse outcomes was 24.2% for VPA when does were at or above the median first trimester dose (i.e. 900 mg/day and was 9.1 % for doses below the median. Meador, K.J. et al. "in utero antiepileptic drug exposure Fetal death and malformations "Neurology 67.3 (2006):407-412. "[V]alproate dose exceeding 1400 per day seemed to be associated with a more steeply increasing malformation rate than at lower does and with a different pattern of foetal malformations." Vajda, F.J. E. and M. J. Eadie "Maternal valproate dosage and foetal malformations" Acta Neurological Scandinavia 112.3(2005): 137-143.; Vajda, F.J. E.et. al. "Foetal malformations and seizure control: 52 months data of the Australian Pregnancy Registry." European Journal of Neurology 13.6 (2006):546-654:

> Higher doses are also associated with a greater likelihood that the offspring will suffer cognitive impairment and developmental delay. "School age children exposed to valproate at maternal doses more than 800 mg daily continue to experience significantly poorer cognitive development than control children or children exposed to lamotrigine and carbamazepine. Baker, Gus A., et al. "IQ at 6 years after in utero exposure to antiepileptic drugs: A controlled cohort study "Neurology 84.4 (2015):382-390. Samren, E. B. et al. *Maternal use of Antiepileptic Drugs and the Risk of Major Congenital Malformations; A Joint European Prospective Study of Human Teratogenesis Associated with Maternal Epilepsy, Elpilepsia*, 38(9):98d1-990, 1997.

8. Opinion

Within a reasonable degree of medical probability, it is my opinion that the major congenital malformation and disabilities, suffered by A.S. including cranial anomalies, facial dysmorphia, cognitive impairment and development delay, are more likely than not, a result of exposure to valproate during Mrs. Sansone's pregnancy, rather than from any other cause. As noted in the many peer reviewed articles cited herein and in appendix B, VPA (Depakote) has a much greater risk factor for causing birth defects (including those seen in this child) than other AED's. This is further compounded by the fact that Mrs. Sansone was taking doses of valproate above 1000 mg a day. As quoted above, the higher the dose, the higher the incidence of valproate related birth defects.

Nathanial H. Robin, M.D. _____

End of report